Third U.S.-Japan Symposium on Cellular and Molecular Aspects of Vascular Smooth Muscle.

Honolulu, Hawaii

February 1-4, 1994

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Seminar Description

1. Scientific Justification:

Insight into the many cellular and molecular processes of vascular smooth muscle described below under "State of the Art Science" is advancing rapidly. Each laboratory in this country and in Japan has many unanswered questions related to the processes. Very predictably other laboratories with this interest have already dealt with some of these problems and will have solutions. The seminar will be a scientific clearing house that will determine problems that now have satisfactory answers. It will identify important problems that are in need of further study.

2. Reason for bilateral support:

Research funds from both the United States and Japan are currently heavily invested in the understanding of vascular smooth muscle function at a cellular-molecular level. The likelihood is great that major and broad advances will be made through this seminar for a relatively small investment. Research in both countries is certain to profit.

3. State of the Art Science

The science of this Joint Seminar deals with the processes involved in the contraction and relaxation of vascular smooth muscle. The cellular processes of excitation, excitation-contraction coupling, energy metabolism and chemomechanical transduction will be analyzed at a molecular level. Regulatory aspects of the endothelium and nerves with regard to vascular function will be featured. The abnormalities of these processes responsible for diseased states will be considered.

In connection with the process of excitation the molecular composition of the membrane and the fluidity of the lipid bilayer will be considered. Characterizations of individual protein channels by the patch clamp technique will be presented. The molecular events responsible for the excitatory process will be defined. These must deal with the agonist-receptor interaction, the post-receptor membrane events and the molecular basis for alterations in membrane potential. Special attention will be given to the "stabilizing" action of bivalent cations on membrane function. Abnormalities in membrane excitability in hypertension will be defined.

Insight into the process of excitation-contraction (E-C) coupling has developed rapidly over the past decade. These developments will permit a definition of the role of the phosphoinositide and cyclic nucleotide systems in the regulation of activator calcium. The control and function of the various types of calcium channels will be considered. The sequestration and release of calcium form the sarcoplasmic reticulum and the plasma membrane will be characterized. The actions of many pharmacological tools in the manipulation of E-C coupling will be presented. These include agents that block or facilitate calcium entry into the cell or that alter the process of intracellular sequestration.

Energy metabolism will be defined in terms of aerobic and glycolytic energy sources. The relative energy cost of synthetic processes, active electrolyte pumping and force generation will be considered.

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In connection with the chemomechanical transduction, the activation of the contractile protein will be considered. What is the relative contributions of a myosin or an actin activated system? What is the role of calcium and of various Kinases in the activation of the contractile proteins?

The role of the endothelium in regulating vascular contractile mechanisms will be given special attention. Most investigators recognize that the endothelium synthesizes both contractile (endothelin, prostaglandins) and relaxant factors (nitric oxide, prostaglandins) but the relative importance of these factors in controlling vascular diameter is not adequately understood. Further, the molecular events that control the stimulation, synthesis and release of these substances is only beginning to surface in the literature.

4. Advantages to both countries:

The United States and Japan are the most productive countries in the world in vascular smooth muscle research. Each will profit from information of current findings presented by the other.

5. Other meetings:

To our knowledge there are no contemporary meetings dealing with the subject of this seminar. In 1977 and 1989, similar bilateral seminars were sponsored by the National Science Foundation and the Japan Society for the Promotion of Science. The products of those seminars were published in Blood Vessels, vol 15, 1978 and in the American Journal of Physiology, vol. 259, 1990. These works have served as an important foundation for much of the research in the area of vascular biology.

6. Timeliness of the proposed seminar:

Molecular and cellular aspects of vascular function will be analyzed with regard to contraction and relaxation. Emphasis will be placed on understanding the regulatory influences of nerves and the endothelium. Many new advances have been made in these specific areas in the last 4 years and they have not been considered in the context of molecular and cellular regulation by a preceding symposium.

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Proposed U.S. Participants and Expected Agenda Topics

Participants	Expected Agenda Topics
Dr. R. Wayne Alexander, Chief Division of Cardiology Emory University 1364 Clifton Rd. Woodruff Bldg, 319 Atlanta, GA 30322 Telephone: 404-727-8147	-Drug receptors, Phoshoinoside signalling
Dr. John A. Bevan Professor and Chairman Department of Pharmacology University of Vermont College of Medicine Given Building Burlington, VT 05405 Telephone: 802-656-2500 FAX: 802-656-4523	-Nerves -Drug receptors
Dr. Mordecai P. Blaustein Professor and Chairman Department of Physiology University of Maryland School of Medicine 655 W. Baltimore St. Baltimore, MD 21201 Telephone: 301-328-3345 FAX: 301-328-8341	-Ion Pumps and Hypertension -Hormonal control
Dr. David F. Bohr, Professor Department of Physiology University of Michigan Medical School Ann Arbor, MI 48109-0622 Telephone: 313-764-4365 FAX: 313-936-8813	-Hypertension, Atherosclerosis, Vasospasm -Energy metabolism, ion pumps

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-Hypertension

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-Intracellular calcium regulation
-Metabolism

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-Drug receptors
-Cyclic nucleotides
-Intracellular calcium regulation

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-Intracellular calcium regulation
-Phosphoinositide signalling

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-Intracellular calcium regulation

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-Intracellular calcium regulation

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-Drug receptors
-Hypertension, atheroselerosis, vasospasm
-Hormonal Control

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Proposed Participants From Other Countries

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Agenda

There will be 12 participants from the United States, 13 from Japan and 5 from other countries. Each of these 30 participants will make a 20 minute presentation followed by a 10 minute discussion. In addition to the 7-8 presentations that will be made each day there will be one hour set aside for general discussion and ample free time for individual discussions.

Tentative Schedule

Tuesday Morning, February 1, 1994

Drug Receptors, Phosphoinositide and Cyclic Nucleotide Signalling

8:30 - 10:00	-	3 presentations
10:00 - 10:30	-	Coffee break (informal discussion)
10:30 - 11:30	-	2 presentations
11:30 - 12:00	-	General discussion

Tuesday Afternoon, February 1, 1994

Membrane potential and ion channels

1:30 - 3:00	-	3 presentations
3:00 - 3:30	-	Coffee break
3:30 - 4:30	-	General discussion

Wednesday Morning, February 2, 1994

Regulation of Intracellular Calcium Concentration

Wednesday Afternoon, February 2, 1994

Regulation of Contractile Protein Activity

Thursday Morning, February 3, 1994

Energy Metabolism and Ion Pumps

Thursday Afternoon, February 3, 1994

Extrinsic Regulartory Systems: Nerves, Endothelium, Hormones

Friday Morning, February 4, 1994

Pathophysiology: Hypertension, Atherosclerosis, Vasospasm

Time schedules for Wednesday and Thursday will be the same as for Tuesday. Friday will have only a morning session. There will be a banquet on Thursday evening.

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